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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,516	12/10/2001	Erwin Houtzager	2183-5208US	8313

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EXAMINER	
WESSENDORF, TERESA D	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 12/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/016,516	HOUTZAGER ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *1-12,14 and 18-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Pri rity under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election of Group II, claims 13 and 15-17 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-12, 14 and 18-39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse.

Status of Claims

Claims 1-39 are pending in the application.

Claims 1-12, 14 and 18-39 are withdrawn from consideration as stated above.

Claims 13 and 15-17 are under examination.

Specification

The disclosure is objected to because of the following informalities: The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See page 2 and page 8, [0023]. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. Applicants are requested to

check for other hyperlink that might be present in the specification.

Appropriate correction is required.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors (typographical, grammatical and idiomatic). Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Information Disclosure Statement

The listing of references in the specification at pages 33-34 is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13 and 15-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide a written description for a method of identifying proteinaceous molecule (synthetic or recombinant) with an altered binding property. The specification does not provide specifics for the numerous different combinations of the undefined variables as claimed. The disclosure provides general definitions of each of the different variables encompassed by the claims. For example, it defines proteinaceous molecule "…in essence, [as] amino acid sequences, …….side chains and/or groups of all kinds may be present……. the amino acid sequence is of less relevance for the structure to design other molecules of nonproteinaceous nature that have the same orientation in space and can present peptidic affinity regions, the orientation in space are the important parameter……" Such definition does not provide specifics that would guide one skilled in the art to the claimed invention

encompassing any kinds of conceivable proteinaceous molecule. The specification at page 28, first incomplete paragraph, recites that "…the most powerful bond is found in sulphide-bridges between two opposed cysteine residues… bacterial cells, in contrast to prokaryotic cells like yeast cells, can have problems with cysteine bridge formations and, therefore, only a limited number of cysteine bridges should be incorporated in proteins that have to be expressed in bacterial cells……" The Examples, which provide the specifics or the adequate written description discloses that products that contain substantial numbers of inosine residues appeared hard to clone and have to be melted to anneal random primers. See page 32, [0087]. Furthermore, it is well known in the art that because of the large molecules of antibodies, even the smallest antigen-binding fragment consists of 250 amino acids. They are composed of two different polypeptide chains which necessitates complicated cloning steps of pair of genes, and in the case of Fv may lead to unstable domain association. They carry six hypervariable loops which are difficult to manipulate at once if the generation of synthetic library is desired. Also, only after the tertiary structures of the protein had been elucidated that the beta barrel can be identified as a loop region that is structurally variable. Thus, there appear to be numerous

restrictions in the design of even a specific protein (not proteinaceous) molecule as immunoglobulin (Ig). The single embodiment provided in the specification, drawn to Ig does not provide adequate written description for the numerous undefined variables of the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13 and 15-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the step between the alteration of the core molecule and the selection steps. It does not recite as how selection of a proteinaceous molecule can be done in the absence of any components from which selection can be made. Furthermore, the preamble recites identifying while the body recites selecting.

B. Claim 16 is indefinite and inconsistent with the base claim. The base claim recites alteration of the proteinaceous molecule which presupposes a post-translational modification such as acetylation. The base claim does not recite the process by which a proteinaceous molecule is produced i.e., by nucleic acid encoding (not coding) the proteinaceous molecule. This step relates more to a process of producing rather than identifying or selecting of the altered binding proteinaceous molecules

Double Patenting

Claims 13 and 15-17 of this application conflict with claims 13 and 15-17 of Application No. 09/316,194. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this

context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 13 and 15-17 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 13 and 15-17 of copending Application No. 09/316,194 ('194 applcaiton). This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The claims in the co-pending '194 application are identical to the present claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13 and 15-17 are rejected under 35 U.S.C. 102(a) as being anticipated by either Skerra (Molecular Biotechnology) or Schlehuber et al (Biol. Chem.) or under 102 (b) over Skerra (WO 99/16873). [As best as the claims can be interpreted].

Skerra discloses at page 257, the abstract, a method of identifying anticalins (proteinaceous molecule, as claimed) by altering the scaffold (core, as claimed) of said anticalcins. The steps includes altering the central element of this protein which is a beta barrel structure of eight antiparallel strands which supports four loops at its open end. These loops form the natural binding site of the chains and can be reshaped by extensive amino acid replacement, thus creating novel binding specificities. The bilin-binding protein (BBP) was employed as a model system for the preparation of a random library with selectively mutagenezied residues. Using phagemid display and colony screening sequences anticalcins have been selected from these library, exhibiting binding activity for compounds like fluorescein or digoxigen. See further page 261, col. 2 and page 263, cols. 1 and 2; Fig. 3 at page 264; Fig. 4, at page 265; Fig. 5 at peg 266 and page 268, Fig. 6. Thus, the specific method steps of Skerra utilizing specific components therein fully meet the broad claimed invention reciting only two broad steps with undefined components therein.

Each of Skerra (WO) and Schlehuber basically discloses the same method as Skerra, above. See the abstract of Skerra (WO patent) and Schlehuber at page 1335.

Claims 13 and 15-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Koide (WO 98/56915 which is equivalent to US 2002019517)).

Koide discloses in e.g., the abstract, a method of selecting catalytic polypeptides by the methods of molecular biology, using both combinatorial chemistry and recombinant DNA. It relates to the generation of polypeptide libraries derived therefrom encoding the molecular scaffolding of Fibronectin Type In (Fn3) modified in one or more of its loop regions (beta barrel, as claimed). It also relates to the "artificial mini-antibodies" or "monobodies," i.e., the polypeptides comprising an Fn3 scaffold onto which loop regions capable of binding to a variety of different molecular structures (such as antibody binding sites) have been grafted. At paragraph [0160] a nucleic acid phage display library having seven variegated residues (residues number 78-84) in the FG loop and five variegated residues (residue number 26-30) in the BC loop was prepared. Variegations in the BC loop were prepared by site-directed mutagenesis using the BC3 oligonucleotide described in Table 1. Variegations in the FG loop were introduced using site-

directed mutagenesis using the BC loop library as the starting material, thereby resulting in libraries containing variegations in both BC and FG loops. The oligonucleotide FG2 has variegating residues 78-84 and oligonucleotide FG4 has variegating residues 77-81 and a deletion of residues 82-84. See further the Examples, which describe the specifics of the invention. Accordingly, the specific process steps of Koide fully meet the claimed invention.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (703) 308-3967. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-7924.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

T. D. Wessendorf
Primary Examiner

Art Unit 1639

Tdw
December 15, 2003